

0103.11
Application No: 10/616,448
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IN THE SPECIFICATION:

On page 22-23, please replace the text under the heading Example 3 with the following:

Example 3

Leuprolide Acetate particles

A single feed solution is prepared under defined conditions. The feed solution is comprised of leuprolide acetate in the aqueous phase of a fluorocarbon-in-water emulsion. The emulsion composition is listed in Table [[3]] 4A below. Accordingly, DSPC and calcium chloride dihydrate are dispersed in approximately 400 mL SWFI (T=60 – 70 C) using an Ultra-Turrax T-50 mixer at 8000rpm for 2 to 5 minutes. The perflubron is then added drop wise during mixing. After the addition is complete, the emulsion is mixed for an additional period of not less than 5 minutes at 10,000 rpm. The resulting coarse emulsion is then homogenized under high pressure with an Avestin C-5 homogenizer (Ottawa, Canada) at 19,000 psi for 5 discrete passes. The emulsion is transferred to the Potent Molecule Laboratory for Leuprolide Acetate addition and spray drying.

Table [[3]] 4A

Leuprolide Acetate Emulsion Composition

<u>Emulsion Components</u>	<u>Amount (grams)</u>	<u>% solids</u>
DSPC	7.33	73%
Calcium Chloride	0.67	7%
Perflubron	200	NA
SWFI	400	NA
Leuprolide Acetate	2.00	20%

Aerosol Data:

Deposition analysis is performed using a multi-stage liquid impinger (MSLI). The apparatus consists of four concurrent stages and a terminal filter, each containing an aliquot of appropriate solvent for Leuprolide Acetate analysis. The powder was administered by inhalation as a dry powder through the Turbospin device (PH&T) at 30, 60, and 90 LPM. The aerosol performance is described below in Table 4B, and the MSLI deposition is profiled in Figure 2. Only a minor dependence of the deposition is observed across a wide range of flow rate.

Table 4B

Flow rate dependence of aerosol properties for a Leuprolide Pulmosphere formulation delivered from the Turbospin DPI device

Q (LPM)	MMAD (μm)	FFP_{4+F} (%)
30	3.3	71
60	2.4	70
90	2.0	63

Little difference is noted in FPF_{4+F} as a function of flow rate, indicating that little dependence in lung deposition would be expected as a function of flow rate.